# CLINICAL TRIALS ADMINISTRATOR

*An essential resource for managers of clinical trials*

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# Compliance alliance: Identify problems, but work with team

*Understand the core factors that cause noncompliance*

Often the best research compliance programs are not the result of overnight inspiration, but are developed through a long, experience-building process.

"Our compliance program is the product of 15 years of experience in the field," says **George Gasparis**, executive director of the human research protection program at Columbia University in New York, NY. Gasparis was a co-author of a research compliance poster presented at the 2009 PRIM&R Advancing Ethical Research Conference, held Nov. 15-16, 2009, in Nashville, TN.

The goal of a solid compliance program is to contribute to an institution's checks and balances with regard to human subjects research. Audits should be done confidentially and with respect for investigators and sites, Gasparis says.

The Columbia University compliance program has a three-step process that begins with investigating to identify noncompliance, auditing study sites to pinpoint problems, and reaching conclusive findings followed by decisive corrective action, Gasparis says.

"Once you identify noncompliance, how do you investigate them in a manner that has integrity, fairness, and comes up with conclusive findings that can be acted upon," he says.

Here is how the program works:

**1. Identify noncompliance:** "It's important that everyone within the operation is able to first recognize something that might be noncompliance and is able to report that efficiently to the compliance team," Gasparis says. "So we have an intake form for reporting an allegation of noncompliance."

Compliance office staff can use forms to provide a quick assessment of potential noncompliance, how the information was discovered, and any additional information.

Columbia uses two forms. One is called the allegations of potential noncompliance reporting form, and the other is a reporting form for research concerns or complaints, says **Jessica Randall**, MA, CIP, an audit


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specialist at the Columbia University IRB.

These internal forms are completed by someone in the compliance office and are used as a guide to obtaining the pertinent information when a caller has allegations of noncompliance. *(See story about reporting forms, p. 39.)*

Part of identification is education. Research staff needs to be taught what constitutes potential noncompliance when these issues should be reported, Gasparis says.

"We train staff for this, and this week we'll have a revised compliance policy on our Web site," he adds.

The policy will have a revised appendix that lists certain common and very minor incidents of noncompliance that should be handled by the IRB and not the compliance office, he says.

"It is more efficient for the IRB to incorporate the consideration of these minor noncompliance examples within their review rather than reporting them to the compliance team," Gasparis says.

These are very specific types of minor noncompliance.

For example, when a human subjects research project is up for renewal, but the investigator has submitted the continuing review paperwork too late and the study lapses, it is noncompliance for any activity to continue on that trial, Gasparis explains.

The appendix specifies that if the research site is analyzing data or continuing to do a minimal risk survey during that period between when the study's IRB approval has expired and before it's renewed, then it's a minor noncompliance issue, he says.

This same example would be considered serious noncompliance if the trial site were to enroll any subjects during the lapsed period, he adds.

**2. Conducting the noncompliance audit.**

Gasparis meets with the compliance oversight team, including Randall, once or twice a week to discuss audit cases.

"We discuss what the allegations are, how we investigate these, how the investigation is proceeding, and how to provide recommendations, follow-up, and monitoring," he says.

The first step is to determine whether an allegation actually has merit.

"First we conduct an inquiry to see if the noncompliance allegation is authentic," Gasparis says. "We do a quick review and pull up a database search."

For instance, if someone has called about a potential noncompliance and gives a common surname for the investigator, it could be the person has the wrong investigator. Or, sometimes, people call about investigators who are at a different institution. So the compliance office checks to make certain any allegations pertain to actual investigators and research at Columbia.

When the noncompliance is genuine, the next step is to see if it requires a full chart review, partial chart review, or some other level of investiga-

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tion.

"Is it appropriate to go on the site and look at files?" Gasparis says.

If a potential noncompliance results in a "yes" answer to any of these three questions then it's likely the case requires an onsite audit:

- Does the study pose greater than minimal risk to subjects?
- Is there the potential that subjects could be harmed?
- Is there very serious noncompliance?

An example of noncompliance that might not require an audit would be one where the investigator reported that he did not document the signed informed consent. But he then gives the compliance office a copy of the IC. A compliance oversight specialist checks the database and sees there are only two subjects enrolled, so the specialist requests a copy of the signed IC for the second subject, Gasparis explains.

"Once we have that form, we have the information we need, and we don't have to go onsite to confirm it," he adds.

For compliance issues that require an audit, compliance officials might decide to first conduct a partial review of records. If the sample reveals a noncompliance trend, then they could decide to conduct a full record audit.

Once an audit date is selected, audit specialists send an audit preparation sheet to the investigator and trial staff. *(See story about audit preparation sheet, p. 40.)*

Then the audit specialist visits the site, using either a not-for-cause audit form or the for-cause audit form, depending on the circumstances.

**3. Document outcomes from the investigation.**

A chief and universal outcome of a noncompliance finding after an audit is to provide education and training to research staff.

"It's essential that every incidence of noncompliance has education and training as one of the actions," Gasparis says. "Something went wrong, and there has to be an awareness of what was wrong and how to do it right."

The goal is to prevent future noncompliance and problematic trends.

"Sometimes we'll recommend researchers use tools, such as Excel spreadsheets, or that they implement processes to prevent this problem from happening again," Gasparis says.

Also, research sites will have to write and implement a corrective action plan (CAP) based on the compliance office's recommendations.

This can include staff changes in events where a noncompliance problem was caused by one individual on the study team. Or it could be a situation where the research site did not have enough resources, so they would have to come up with a plan for hiring additional staff, he suggests.

"Maybe there was a breakdown in the process and simply implementing a couple of key strategies would prevent it from occurring again," Gasparis says. "So it's important to understand the core factors that cause the noncompliance and come up with a solution to prevent it from happening again."

For instances of serious noncompliance, audit specialists will put the research site on a schedule for monthly audit checks to ensure the CAP has been implemented, he adds.

"Or we may expand the audit to other studies by that investigator," he says.

A compliance program's auditors should keep in mind that not all investigations end with findings of noncompliance, Gasparis notes.

"Sometimes one will find through an investigation that a study actually was conducted very well," he says.

"So it's important that one does not assume that someone is guilty until the investigation is conducted," he adds. "And you should preserve the reputation of the researcher or research team." ■

# Capture the details: Key compliance facts and questions

The first step in finding any research noncompliance is to identify it, and the most efficient method for this is to make it easier for research staff, investigators, and study participants to report their concerns.

"We have more and more self-reports of noncompliance each year simply because people see that we work with them to correct noncompliance issues rather than imposing sanctions that would be inhibitive to their research," says **George Gasparis**, executive director of the Columbia human research protection program at Columbia University in New York, NY.

Of course, any serious noncompliance must be reported to regulatory authorities, including the FDA and/or Office of Human Research Protection

(OHRP), he adds.

The compliance office uses a form for research staff to complete when they have a noncompliance concern. It's called the Columbia University IRB's "Reporting of Allegation of Research Noncompliance or Protocol Deviations Requiring Compliance Oversight."

It's a simple, one-page check-box form that asks for information that includes the following:

• Date of notice, IRB protocol number, IRB of record, principal investigator, study title, protocol level of review, name of individual providing this notice;

• Nature of the event:

- Failure to obtain IRB approval prior to conducting human subjects research;

- Recruitment of study subjects during a period of lapsed IRB approval;

- Performance of study-related procedures or data analysis during a period of lapsed IRB approval;

- Enrollment of subjects in a study without obtaining legal effective informed consent;

- Failure to report/late reporting of serious or recurring problems involving risks to human subjects;

- Protocol deviations requiring COT investigation;

- Dosing errors;

• Please provide a description with sufficient details of the event.

There also are check-boxes for listing actions taken by the board and compliance office. And the form lists the names and e-mails of the compliance oversight team.

The compliance oversight program also has a form that can be used by compliance staff to focus their questions when someone calls with a study concern or complaint. It's called the Columbia University IRB's "Reporting Form for Research Concerns or Complaints."

The form has two pages and provides check-boxes and sections for information.

"We capture the information on the form and begin looking into the situation to see if there really is noncompliance that needs to be investigated," says **Jessica Randall**, MA, CIP, an audit specialist at the Columbia University IRB.

"We begin to track the situation, using the form," she adds.

"The form has specific questions the person taking the call can ask," she explains. "Someone might not think to tell us what the research protocol number is, or they might not remember the doctor's name."

Here are some items included in the form:

• Name or initials;

• May we reveal that you are the source of this concern or complaint to the study's principal investigator and other study staff?

• Are you making this report for someone else?

• Contact information is required for follow-up: phone, alternate phone, e-mail address, other contact info;

• Please tell us about the study for which you have a concern or complaint: study name or description, name of principal investigator;

• Please tell us about the research concern or complaint you are reporting;

• Please tell us how you would like to see your concern or complaint resolved;

• Have you discussed this concern or complaint with the principal investigator or other study staff? If yes, please let us know who you contacted;

• Are you or were you a participant in the study?

• When (approximately) did you start participating in the study?

• Are you still participating in the study?

There also is a section for the person who handled the call to write down the date the call was received, date it was entered to tracking log, resolution date, who it was referred to, and detailed study information. ■

# Compliance office gives PIs audit preparation sheet

*'Knowing you're about to audited can be scary'*

Compliance officials can call principal investigators (PIs) and let them know about a scheduled audit, but chances are the site will be inadequately prepared for an efficient audit visit.

One solution is to send PIs a letter that details what will be happening and what the audit specialist needs to complete the oversight visit.

Columbia University of New York, NY, has a one-page audit preparation sheet that explains what the compliance oversight team needs the site to do for the audit, says **Jessica Randall**, MA, CIP, an audit specialist at the Columbia University IRB.

"For most investigators knowing that they're about to be audited can be a scary experience, whether it's for-cause or not-for-cause," she adds. "So this sheet lets them know what to expect, including the space we'll need, who the auditor will be, the information the auditor will need, such as regulatory binders, subjects binders, and names of everyone enrolled in the study."

The goal is to develop trust and help investigators and clinical trial coordinators prepare for the audit visit, Randall says.

"We make sure everything is taking place in accordance with regulations," she says.

Since Randall began using the audit preparation sheet, she has seen improvement in site preparation for audits.

"People can reference the audit preparation sheet, and it's easier for us to hand them this than to have to explain everything over the phone," she says. "There is no ambiguity, and we know they can contact us if they have any questions."

Here are some features of the audit preparation sheet:

• It requests PIs and clinical research staff to have these items ready for the audit:

- Space, including seats and table, for one or two audit specialists for a four-hour block of time in a private area near study files;
- Access to a coordinator or study team member who has intimate knowledge of the research study under audit;
- Fifteen minutes of the PI's time at the beginning of the audit to go over the scope of the audit and to answer any questions the PI may have;
- A copy of the enrollment log for the audit specialist to use. This would include a list of all subjects enrolled and their study ID number, including those who were screen failures, excluded, or dropped out;

• The form lists a sample of items the compliance oversight team will need easy access to, including these:

- Regulatory binder;
- IRB approval letters, stamped questionnaires, stamped consent forms, advertisements, and correspondence;
- Sponsor protocol and correspondence if applicable;
- Subjects charts, subjects signed consents, subjects signed HIPAA forms;
- Queries, monitoring reports and resolutions, outside audit reports.

• For FDA studies, these also need to be made available:

- All FDA correspondence and FDA approval letters;
- IND/IDE paperwork;
- Drug logs, drug shipping logs;
- Sponsor correspondence;
- Data monitoring committee reports, if applicable;
- Investigational brochure;
- Monitoring visit reports.

• The form concludes with a reminder that all correspondence — from the audit, the subsequent report from the compliance oversight team, and the PI response — should be filed in the regulatory binder at the conclusion of the audit. ■

# Why do some potential CR subjects decline studies?

*NIMH has some answers*

Clinical trial sites go to a great deal of trouble to identify potential research participants, screen them, and then provide the necessary informed consent before they are enrolled in studies. But at some point in the process a proportion of potential volunteers say they're not interested.

Why? And how do you salvage some of this potential recruitment pool?

The main reason listed for why people ultimately decline to participate has to do with protocol procedures, according to data collected by the National Institutes of Mental Health (NIMH) of the National Institutes of Health (NIH) in Bethesda, MD. NIMH has data from over a decade of screening interested volunteers who decided after being pre-screened that they were not interested in participating in a study.

The NIMH data include people who voluntarily called about studies after seeing or hearing advertisements.

"The screens we completed from 1999 until the present identified patterns in the public, and, of course, we made many referrals to studies," says **Julie Brintnall-Karabelas**, MSW, LCSW-C, clinical research advocate of the human subjects protection unit of the Office of Clinical Director at NIMH. Brintnall-Karabelas and co-researchers presented an abstract with their findings at the

2009 PRIM&R Advancing Ethical Research Conference in Nashville, TN.[1]

"However, a unique group stood out, and this is why we decided to study recruitment," she says. "This is a group of individuals who called us, expressed an interest in participating, and they were eligible; however they declined participation."

NIMH had 965 people who were eligible, but who declined participation. These potential participants had a wide-range of diagnoses, including autism, Alzheimer's disease, anxiety, depression, bipolar disorder, obsessive compulsive disorder, post-traumatic stress disorder, and schizoaffective disorder.

"This is new territory and rarely has been explored," Brintnall-Karabelas says. "There isn't much information out there about eligible participants who decline."

Here are the trends investigators found:

- 36% declined to participate because of protocol issues;
- 33% declined to participate due to inconvenience or lifestyle issues;
- 26% declined for other, non-specified reasons;
- 3% declined for financial reasons;
- 2% declined because they would like to participate in research elsewhere.

## Recommendations for action

Investigators reviewed these findings and came up with a number of recommendations that researchers might follow to help improve their clinical trial recruitment. *(See recommendations for CT recruitment, p. 43.)*

The study was limited in its ability to further breakdown the reasons for declining to participate, but there were some trends, Brintnall-Karabelas says.

For example, those who declined for financial reasons were people who said they'd only participate in a study in which participants were paid, and the study for which they were eligible lacked the compensation they desired, she says.

Also, the 21 people who said they would participate in research elsewhere were mostly people who had responded to advertising about a particular study of repetitive transcranial magnetic stimulation (RTMS) to treat depression. When they found out they were eligible for a different study, but not for an RTMS study, they declined to pursue an RTMS study elsewhere, she adds.

For some of the potential participants, the protocol issues and inconvenience issues overlapped.

Some NIMH studies require lengthy inpatient stays of two months to nine months, Brintnall-Karabelas says.

"One of the things mentioned was the length of the study was too long," she says.

Some individuals who listed protocol reasons for declining had said they did not want to participate in a randomized, placebo-controlled trial because they were worried about being given the placebo, she says.

Another protocol issue involved the required wash-out period, which is the time a person who has been on medications takes to stop using drugs and let them wash out of his body," she explains.

"Some people expressed concern that their symptoms would get worse due to the wash-out of their medication," Brintnall-Karabelas says. "Some expressed an unease about the length of time spent in the MRI or the PET scans, and these might be related to claustrophobia."

Others had concerns about radiation exposure from the PET scans or having an arterial line placed in them or the medication side effects, she adds.

For a number of people in the inconvenience category, the issue was an inability to take time off of work to lack of transportation to get to the center.

So some of the concerns could be addressed with education or by other means, and some of the interviewers conducting the screening calls were able to change people's minds, Brintnall-Karabelas says.

For instance, if someone expressed concern about the MRI, then the interviewer might suggest they take a look at the MRI and see if they'd be comfortable with it. Or if someone is concerned about radiation from the PET scan, then the interviewer might let them know that it raises their risk of cancer in their lifetime from 25% to 25.03%, Brintnall-Karabelas suggests.

The study had no clear data on the people who didn't have a clear reason for declining participation, but some of the anecdotal evidence suggested a variety of reasons, such as symptom remission, concern about confidentiality, and an interest solely in homeopathic or alternative remedies, she says.

"For the inpatient studies, some people were concerned about losing their housing or losing their jobs," she adds. "However, NIH and NIMH have a large interdisciplinary team that has a specialization of social workers who can help partici-

pants maintain housing and work."

Often the concerns people have can be addressed through further education, Brintnall-Karabelas says.

"Education can really influence whether some people participate or not," she adds.

REFERENCE

1. Brintnall-Karabelas J, Cadman ME, Sung S, et al. Improving recruitment in clinical trials: why eligible participants decline. Abstract presented at the 2009 PRIM&R Advancing Ethical Research Conference. Nov. 14-16, 2009. Nashville, TN. ■

# Relooking at refuseniks: Why did they say no?

*Educate, make flexible study protocols*

Often investigators can improve their clinical trial recruitment numbers by simply spending a little more time on education during the screening process, according to an expert.

Researchers at the National Institutes of Mental Health (NIMH) of the National Institutes of Health (NIH) in Bethesda, MD, have collected a decade's worth of subject recruitment, including screening interviews.

Potential participants were screened and carefully questioned when they proved to be eligible, yet many still declined to enroll in a clinical trial, says **Julie Brintnall-Karabelas**, MSW, LCSW-C, clinical research advocate of the human subjects protection unit of the Office of Clinical Director at NIMH.

Brintnall-Karabelas and co-researchers saw some potential in their data. What if they could identify trends in why people declined to participate and then use these to develop recommendations that might help improve future recruitment?

So they reviewed data, found several main reasons that people declined participation and came up with these general recommendations:

**1. Increase awareness and education.**

"The interdisciplinary team members who have initial contact with potential participants should have specialized training so they're equipped to answer any questions or concerns during the screening or recruitment process," Brintnall-Karabelas says.

"They should provide information to callers through verbal discussions or sending them health education brochures or fact sheets or links on the Internet," she adds. "This can alleviate people's concerns and answer their questions about research participation."

For example, there is a free, 25-page brochure available through NIMH, called "Participants' Guide to Mental Health Research." (It's publication 08-4379 and can be downloaded at www.nimh.nih.gov.)

"It is about the nuts and bolts of research," Brintnall-Karabelas says. "It answers basic questions about clinical research, including what rights I have, what is randomization, what is informed consent, and what is your alternative to research."

**2. Build flexibility into study protocols.**

Some potential study participants are skeptical of being involved in randomized, placebo-controlled trials because they don't want to be given a placebo.

So investigators who design protocols to have a second arm in which even the placebo cohort receives treatment might find that this increases enrollment, Brintnall-Karabelas says.

"A solution is to offer cross-over studies where there might be an arm of the study where you have a 50-50 chance of getting treatment or placebo," she explains. "But once you complete the first arm, then you can get actual treatment in the second arm."

This type of protocol design might be more appealing to some participants and draw in people who otherwise would decline to enroll.

"The more options offered to participants, the better," Brintnall-Karabelas says.

"There also are studies that allow participants to have an opportunity to make the choice to either be in an open label treatment study where they get the medication, participate in a placebo-controlled arm, or cognitive behavioral therapy," she adds.

"Flexibility is the key," she says. "People are more likely to participate in protocols that have options or have cross-overs."

Researchers should keep in mind that during the initial stages of protocol development, the public's perceptions are important. While a trial cannot be too flexible, it also cannot be too rigid, Brintnall-Karabelas says.

"Whenever possible, tweak studies to accom-

modate subjects," she adds. "Is it a good sample if you're leaving out a certain group because of extremely rigid inclusion/exclusion criteria?"

**3. Address potential participants' concerns when possible.**

There are actions both simple and more complex that clinical trial sites can take to reduce the burden of research involvement for participants.

For example, one solution to reducing the time-consuming paperwork portion of participants' study visits is to have them complete some of this initial paperwork and admissions forms before they have their first visit, Brintnall-Karabelas suggests.

They could complete some of this paperwork through encrypted e-mail, she says.

Also, it helps participants if a clinical trial site can offer after-work study visit hours.

"At NIMH, participants are very enthusiastic about coming to the clinical center after work at 5 o'clock or doing an MRI on Saturday morning," Brintnall-Karabelas says. "These appointments fill up right away."

Another solution might be to offer participants the option of an open MRI if they're claustrophobic and are reluctant to participate if a closed MRI is required, she adds.

And CR sites should consider participant compensation for studies, if they don't already do so.

"Remember that people are interested in studies that provide compensation," Brintnall-Karabelas says.

Lastly, CR sites could collect their own data on why people decline to participate, and these answers might provide clues that lead to solutions, she advises.

"I think the research community is really good at maintaining data regarding participants," she says. "But they also should maintain data on nonparticipants and those who withdraw from studies." ■

# Error-free billing: A best practice model

*Key is proactive analysis of charges*

Aurora Health Care of Milwaukee, WI, has had a very good track record in research billing compliance in recent years, and its success can be attributed to its billing compliance best practice model.

"Aurora Health Care's research billing compliance program is as much about analysis done before services are ever delivered as the correct process afterwards," says **Geoffrey Schick**, MBA, director, clinical trials research for Aurora Health Care.

"We invest considerable time and effort in mapping out and determining all services and whether they're billed and billable," he says. "That's key to our system, and the time and effort invested keeps us comfortable that we're abiding by guidelines and rules."

Also, the health system errs on the side of caution since research, although considerable, is a small piece of the organization's overall revenues, he adds.

The 15-hospital health system has an average of 250 open clinical trials.

"The backbone of our research billing compliance program is Medicare coverage analysis," Schick says. "We take the protocol and break down all the services into components by CPT code or charge code, and we have trained staff analyze the code and services, sifting through a mountain of data to see if services are billable by Medicare."

This task is handled by the medical audit department.

"They ultimately make a determination if something is billable or not," Schick says.

The medical audit department is comprised of specially-trained staff, typically that have a decade or more of experience in nursing, he says.

The hospital developed the system after receiving recommendations from a consulting firm.

"We have one medical auditor who was originally trained by the consultants, so when we add a new medical auditor we are able to train internally," Schick says.

The medical auditors are very thorough in their proactive assessment. Here are the chief ways they ensure that every potential protocol charge is correctly assessed:

• Medical auditors review available guidelines, coverage decisions.

The auditors look at investigative procedures or interventions to see what's already available and to get an idea of the patient population.

Then they look at the Medicare guidelines, local coverage decisions that apply to the region, and they look at medical society Web sites to see if any of the published guidelines might apply, Schick

says.

"They want to see if published guidelines could be used for justification that a service should be standard of care," he says. "If there's published evidence-based justification behind it, then it helps us make a decision that this should be done."

It's particularly helpful when medical societies have up-to-date guidelines, he adds.

"But if there's some period of time where people have not updated their Web pages, or if certain services are done routinely, then it's different," Schick says. "If the medical society hasn't updated its Web pages, then we don't have the documentation we need to say we agree that this is okay to bill as routine care."

• Teach difference between routine care and what Medicare covers as standard of care in research.

Physicians sometimes mistake the two.

"There are many cases where what a physician does as standard of care may be perfectly reasonable and billable for insurance programs, but it doesn't mean that it's standard of care for research purposes," Schick says. "They might bill for this many times and it's always accepted, but once you get into the research world, there's a higher level standard."

Physicians have to support what they consider routine care in research, providing a reason why this is routinely done and documenting this explanation, he adds.

"It's the science of medicine, but we have to abide by all the rules and regulations," he says.

For instance, investigators need to document the research participant's clinical indications, signs and symptoms.

It's also wise to teach clinical trial coordinators about the difference between what is routine practice in clinical medicine and what is considered standard of care for Medicare billing in research.

"Since 85% of our physician investigators' day is routine clinical care, we need clinical coordinators who assist in the delivery of care to be just as aware," Schick says.

"Our philosophy is to provide the service, document the reason behind it, and we'll either bill or not bill depending on what's there," he says.

• Medical auditors use checklist as guide.

Aurora's medical auditors use a clinical trials coverage analysis checklist to guide their decisions.

"The checklist is a process of following stipulations spelled out in Medicare national coverage decision," Schick says. "We collect information, including the IND number, different steps, protocol-specific questions, and information about gaps in identifying Medicare coverage."

For example, the checklist has a section in which the medical auditor can write about billing issues, spelling out specific precedents and concerns.

Also there are a number of questions that can be answered with a "yes" or "no," including these:

- Is this a Medicare Deemed Qualifying Trial?
- Does the coverage analysis outcome indicate proceeding with trial?
- Does an approved Medicare benefit category exist for the services to be provided in this trial?
- Does this trial have therapeutic intent?
- Will this trial enroll healthy patients?
- Is this a diagnostic intervention enrolling healthy patients as a control group only?
- Federally funded?
- Conducted by Centers or Cooperative Groups and the trial is funded by a Federal agency?
- Drug trial with an Investigational New Drug (IND) number assigned by the FDA?
- Does a specifically applicable National Coverage Decision (NCD) exist?
- Is the specific NCD a non-coverage decision?

"Once you identify these things, then the next step is making a decision and moving forward," Schick says. "These decisions aren't low dollar costs, so you might not feel it's ethical to ask subjects to bear the cost of it."

• Explain decisions to sponsors and negotiate changes in budget.

"Some sponsors are extremely knowledgeable and very good and practical in terms of what the initial budget offers," Schick says. "But a majority of sponsors typically offer a low rate, gravitating toward the Medicare reimbursement level, and often they don't understand the Medicare billing rules in terms of standard of care."

Sponsors frequently rely on national principal investigators to define standard of practice, although these decisions might not match with what Medicare allows.

"I had a conversation with a sponsor at a conference, and I said, 'Why don't we talk more? Why don't you hire our medical audit team to look at your contracts to see what's billable and what's not?'" Schick recalls. "He said, 'What's in it for us? If we offer low dollars, and everyone takes it, we win. If they don't take it, then no sponsor is called on the carpet for this.'"

The lesson is that sponsors do research as part of their business and treat it as such. So it's up to clinical trial sites to carefully assess protocols and

budgets and ask for more money when they know they won't be reimbursed by Medicare for particular interventions.

• Keep communication lines open and checks and balances.

It's important to have layers of checks and balances, so any thorough compliance program should have clear, open lines of communication between all parties involved in research and research compliance.

"We've evolved into a very strong research billing compliance program based on prospective analysis," Schick says.

"And the other part is having good communication between hospitals and clinics and the research billing team," he adds. "We make sure we catch all research subjects' accounts for final review and processing to make sure [nothing that should be billed to research] is paid by third-party payers."

Research billing staff review all research subjects' accounts before the accounts are processed by the regular billing staff, he says.

The four medical auditors work primarily on prospective analysis, although they're available to handle a resolution when there's a research billing question or when something did not work according to the protocol or needs further analysis.

Another four employees handle research billing for a total of eight people dedicated to research billing, Schick says.

"They all work with the department of clinical research, but they don't work for the department of clinical research," he says. "It's part of the checks and balances, and their findings are independent and not influenced by what I think might be a good study." ■

# Rework informed consent to improve subjects' understanding

*Ask thorough questions as part of IC*

Research professionals increasingly are aware of how important it is to assess and anticipate research volunteers' comprehension before writing informed consent documents. Still, the industry is lagging behind the reality, an expert says.

"There are some very influential groups, including professional and nonprofessional groups, who are trying to raise the awareness," says **Kris Walters**, PhD, MSM, clinical research program coordinator at the University of North Carolina in Wilmington, NC.

"The other reason why I believe awareness of consent is an issue is because the FDA also is citing informed consent a little bit more, and they're looking into the clinical research (CR) processes more," she adds.

"The flip side is although I see a trend with clinical research sites being a little more aware of comprehension and consent, we're still very far away from sites really improving the informed consent process," Walters says.

Some nonprofit organizations have been working to raise overall public awareness of the CR process and patients' rights, she notes.

Theoretically this means when patients are approached about volunteering for a CR trial they'll have a better understanding of their alternatives and make a more educated or informed decision.

Yet there still are problems, especially in the areas of writing informed consent forms at a lower reading level and providing more time to allow patients to understand the forms, Walters says.

Too often CR sites follow this routine informed consent process: "They provide the patient with the informed consent form. Then they leave them in a room for a while to allow them time to read the consent form uninterrupted. When they return to the patient, they ask, 'So, do you have any questions about what you read?'" Walters says.

And that's where the informed consent process ends.

"They're not actually assessing whether the patient truly understands what he's read," she says.

"Some principal investigators (PIs) say, 'Well, we've given them that opportunity, and that's all we're supposed to do,'" she notes. "But it's also the PI's responsibility to assess the patient's ability to understand what he's volunteering for, and you do this by spending more time with the patient after the patient has read it."

Then the PI or CR coordinator should quiz the patient, asking pointed questions, Walters suggests:

They can say to the potential research participant: "Okay, we want to make sure you understand. Are you interested in this study?" Walters

says. "If you are interested, we want to make sure you understand what you're volunteering for, and so I want to ask you a few questions about what you've read."

## Key questions

These questions could be as follows:

- Do you understand this is a research study?
- Do you remember who to call if you have any questions about your rights as a volunteer for this study?
- We want to make sure you understand more about some of the adverse reactions you might have by taking this investigational product. Can you name some of those that you read about in the consent form so we can be sure you understand that?
- Did you read that there would be any benefit to you?

"If the patient says, 'yes,' while the informed consent form explicitly says there is absolutely no benefit, then the PI or coordinator should probe further, Walters says.

For instance, potential participants often think a benefit is that they'll be paid for participating in the study, and if they indicate that's the benefit they read about, the PI might ask, "Other than getting paid, do you remember if there's any benefit to you in participating in the trial?" Walters suggests.

"That's very important to ask because many people have a false hopes syndrome, especially if they're suffering from a serious disease," she explains. "So even if they're told there is no direct benefit from the study, they'll still believe they'll get a benefit from it because this is a new product."

Another area that needs improvement is the actual informed consent document's size and reading comprehension level, Walters says.

"The average American reads about two sentences before the attention span is diverted in some way," Walters says. "Informed consent forms still are seven to 10 pages long, so there's a disconnect between how people are communicating in the written form today."

With the popularity of Twitter and text messaging, there's a huge disconnect between the way people commonly receive information in the electronic information age and how information is conveyed in the standard informed consent form, she adds.

"So one way we can try to make that connection is to spend more time as clinical coordinators and researchers gently asking questions about what they've read," Walters says.

Research volunteers who understand the study and process more fully also are more likely to stay enrolled and stay adherent to the protocol regimen.

"The important reason why you want to do this is because the better the patient understands what the study is about and why they're a candidate," she says. ■

## CNE/CME OBJECTIVES / INSTRUCTIONS

The CNE/CME objectives for Clinical Trials Administrator are to help physicians and nurses be able to:

- review pertinent regulatory mandates;
- develop practical clinical trial oversight strategies;
- review best practices shared by facilities that successfully conduct clinical trials.

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you.

## COMING IN FUTURE MONTHS

- Research program creates 15 educational modules for CR
- CR participants discuss what means most to them
- Here's a look at OHRP compliance oversight issues
- Improve data queries, data cleaning
- Make best use of recruitment marketing dollars

# CNE/CME QUESTIONS

13. What is the first step in a thorough noncompliance, for-cause audit?
    A. Notify principal investigator of date of site visit
    B. Determine whether an allegation has merit
    C. Notify the FDA of the complaint
    D. None of the above

14. According to a study conducted by the National Institutes of Mental Health, which of the following is a chief reason why potential subjects decline to participate in a study?
    A. They declined to participate because of protocol issues
    B. They declined to participate due to inconvenience or lifestyle issues
    C. They declined to participate due to financial reasons
    D. Both A & B

15. To improve billing compliance, a medical research auditor checklist might ask all but which of the following?
    A. Is this a Medicare Deemed Qualifying Trial?
    B. Does the coverage analysis outcome indicate proceeding with trial?
    C. Will Medicaid cover the intervention if private insurance does not?
    D. Does an approved Medicare benefit category exist for the services to be provided in this trial?

16. Which of the following is one of the chief problems with the typical research informed consent process?
    A. Investigators fail to ensure that subjects fully understand the purpose of the protocol and their rights, risks, and potential benefits
    B. Informed consent documents contain too little pertinent information
    C. Informed consent documents fail to clearly state that the subject might receive no personal benefits from the trial
    D. All of the above

**Answers: 13. B; 14. D; 15. C; 16. D.**